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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,427	11/14/2001	Avi J. Ashkenazi	P2730P1C10	4110

35489 7590 04/19/2004

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,427	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-118 were cancelled, and new claims 119-124 were added in the Preliminary Amendment filed 11/14/2001.

Priority

According to the priority statement of 11/14/2001, it appears that priority is being claimed to a large number of utility and provisional applications. These applications appear to be drawn to unrelated subject matter and are either not available for consideration or for which consideration to determine support for the instantly claimed subject matter would require an undue burden. Accordingly, the subject matter defined in claims 119-124 has an effective filing date of 11/14/2001, that of the instant application.

Applicants are requested to provide the serial number and specific page number(s) of any parent application to which priority is desired which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled of prior to 11/14/2001.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Information Disclosure Statement

References A1 and A2 on the IDS submitted 5/24/ 2002 have been lined through because they are not in the correct format. The citation should include the author and publication date, pursuant to 37 CFR 1.98.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-124 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance, thus there is not a patentable utility for antibodies which bind the protein. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The data in the Specification show that gene expression is increased in tumor cell lines and primary tumors. No data is presented regarding the levels of protein expression. It does not necessarily follow that a decrease in copy number of the mRNA results in a change in protein expression that would correlate to the disease state, and thus it does not follow that an antibody

to the polypeptide would correlate to the disease state. Haynes et al. (Electrophoresis 19:1862-1871, 1998) studied 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein sand transcript levels; for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50-fold. Haynes concluded that the protein levels couldn't be accurately predicted from the level of the corresponding mRNA transcript (page 1863, second paragraph and Figure 1).

The Specification additionally sets forth that the PRO830 is homologous to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

After complete characterization, the protein may be found to have a patentable utility, and thus an antibody that binds this protein would have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to an antibody that binds a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO830, the instant invention is incomplete. The polypeptide encoded by the nucleic acids of the instant invention is alleged to be structurally analogous to proteins that are known in the art as, *inter alia*, HSU88154. In the absence of knowledge of the natural substrate or biological significance of this protein, there is

no immediately obvious patentable use for it. To employ an antibody that binds a protein of the instant invention in the identification of substances that inhibit the proteins activity is clearly to use it as the object of further research that has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for PRO830 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 119-124 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

35 U.S.C. §§ 102 and 103

The following rejections under 35 U.S.C. §§ 102 and 103 are made under the assumption that the effective filing date for the instantly claimed invention is 11/16/2001, which is the actual filing date of the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 119-120, 122-124 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,169,933 (Anderson et al.).

The '933 patent discloses covalently linked complexes comprising antibodies to a peptide which has a region of 8 amino acids 100% identical to SEQ DI NO: 175 (see Sequence Comparison A, attached). These antibodies would cross-react to SEQ ID NO: 175, thus claims 119 and 124 are anticipated. The '933 patent also discloses monoclonal antibodies, and labeled antibodies (column 4, lines 3-11), thus claims 120, 123 are anticipated. The '933 patent also discloses antibody fragments (column 3, lines 50-53), thus claims 122 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 119-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,169,933 (Anderson et al.) in view of U.S. Patent No. 5,530,101 (Queen et al.).

The disclosure of the '933 patent has been set forth above. The '933 patent differs from the instant invention by not disclosing humanized or single-chain antibodies to the polypeptide. U.S. Patent No. 5,530,101 discloses that non-human antibodies do not fix complement as well as human antibodies, thus necessitating the humanization of antibodies produced in other species (column 1, line 38), this also indicates the superiority of human antibodies. U.S. Patent No. 5,530,101 discloses the humanization of antibodies (column 2, lines 1-8). Humanized antibodies are disclosed as being important because they bind to the same antigen as the original antibodies,

but are less immunogenic when injected into humans. U.S. Patent No. 5,530,101 discloses that immunoglobulins may exist in a variety of other forms, including, *inter alia*, single chains. Therefore, it would have been obvious to one of skill in the art at the time the invention was made to humanize antibodies which bind SEQ ID NO: 175.

Conclusion

Claims 119-124 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
April 7, 2004

Sequence Comparison A

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RESULT 1
5169933-6
;Patent No. 5169933
;    APPLICANT: ANDERSON, DAVID C.;MORGAN, CHARLES JR.;FRITZBERG,
;ALAN R.;NICHOLS, EVERETT J.
;    TITLE OF INVENTION: CAVALENTLY-LINKED COMPLEXES AND METHODS
;FOR ENHANCED CYTOTOXICITY AND IMAGING
;    NUMBER OF SEQUENCES: 45
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/07/390,241
;      FILING DATE: 07-AUG-1989
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER: 232,337
;      FILING DATE: 15-AUG-1988
;SEQ ID NO:6:
;      LENGTH: 14
5169933-6

  Query Match             9.2%;  Score 8;  DB 6;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 0.17;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         18 LVGFLLLL 25
              ||||||||
Db          5 LVGFLLLL 12
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